

ORIGINAL ARTICLE

Prior inpatient admission increases the risk of post-operative infection in hepatobiliary and pancreatic surgery

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Abstract

Background: Hepatobiliary and pancreatic (HPB) operations have a high incidence of post-operative nosocomial infections. The aim of the present study was to determine whether hospitalization up to 1 year before HPB surgery is associated with an increased risk of post-operative infection, surgical-site infection (SSI) and infection resistant to surgical chemoprophylaxis.

Methods: A retrospective cohort study of patients undergoing HPB surgeries between January 2008 and June 2013 was conducted. A multivariable logistic regression model was used for controlling for potential confounders to determine the association between pre-operative admission and post-operative infection.

Results: Of the 1384 patients who met eligibility criteria, 127 (9.18%) experienced a post-operative infection. Pre-operative hospitalization was independently associated with an increased risk of a post-operative infection [adjusted odds ratio (aOR): 1.61, 95% confidence interval [CI]: 1.06–2.46] and SSI (aOR: 1.79, 95% CI: 1.07–2.97). Pre-operative hospitalization was also associated with an increased risk of post-operative infections resistant to standard pre-operative antibiotics (OR: 2.64, 95% CI: 1.06–6.59) and an increased risk of resistant SSIs (OR: 3.99, 95% CI: 1.25–12.73).

Discussion: Pre-operative hospitalization is associated with an increased incidence of post-operative infections, often with organisms that are resistant to surgical chemoprophylaxis. Patients hospitalized up to 1 year before HPB surgery may benefit from extended spectrum chemoprophylaxis.

Received 17 April 2015; accepted 16 July 2015

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Introduction

Hepatobiliary and pancreatic (HPB) resections are complex operations associated with a high incidence of post-operative morbidity. Post-operative infections constitute the largest proportion of post-operative morbidity and are strongly associated with long-term oncological outcomes, including the time to initiation of chemotherapy, recurrence and overall survival.^{1–3} Post-operative infections also impose a considerable financial burden to both hospital and patient by increasing the hospital length of stay, utilization of resources and readmission rates.⁴

This study was presented at the 9th Annual Academic Surgical Congress, 4–6 February 2014, San Diego, California.

Development of a surgical-site infection (SSI) can extend the duration of hospitalization by up to 10.6 days and cost an additional \$20 842.^{5,6} Collectively, post-operative infections impose considerable and potentially preventable costs exceeding \$900 million and hospital readmissions accounting for an additional \$700 million in healthcare expenditures.^{5,7}

Prior hospitalization may place patients at a higher risk of colonization with hospital-associated organisms that could lead to post-operative infection after HPB surgery. Prior hospitalization is associated with increased incidence of resistant hospital-associated infections and *Clostridium difficile* colonization among patients admitted to surgical and non-surgical wards.^{8,9} Furthermore, patients colonized with one resistant pathogen are frequently colonized with other resistant organisms;

methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE) and other multi-drug resistant organisms have been reported.^{10–12}

Many patients undergoing HPB surgery are admitted to the hospital prior to surgery for diagnostic testing or therapeutic interventions. Regardless of pre-operative hospitalization status, these patients receive standard peri-operative prophylaxis. However, these drugs possess antimicrobial spectra that may fail to protect against these resistant, hospital-acquired pathogens. In this study, it is hypothesized that a prior hospital admission increases the risk of a post-operative infection in patients undergoing HPB surgery. It is also hypothesized that patients sustaining infections are infected with microorganisms that are resistant to peri-operative antimicrobial prophylaxis.

Patients and methods

Study design and patient selection

We conducted a retrospective cohort study of all adult patients (≥ 18 years) who underwent HPB surgery at the University of Pittsburgh Medical Center between 1 January 2008 and 1 July 2013. These surgeries include: minor and major liver resections; bile duct reconstructions/resections; central and distal pancreatectomies; pancreaticoduodenectomies; pancreatic enucleations; and liver radiofrequency ablations. Data for each surgery had been prospectively collected for an institutional clinical registry. To ensure accuracy, registry data were cross-referenced with operating room logs. Patients who previously underwent organ transplantation or had multiple HPB surgeries were excluded. Those without post-operative infections who did not survive to post-operative day 30 were also excluded.

Our primary exposure of interest was pre-operative hospitalization, which was defined as any hospital admission occurring up to 1 year prior to the index operative admission based on other studies that identified prior hospitalizations up to 1 year as a risk factor for carriage of resistant organisms and as a risk factor for being admitted with a resistant infection.^{8,13–15} The present primary outcome of interest was post-operative infection within 30 days of surgery as defined by Centers for Disease Control's (CDC) standardized definitions of HAIs and SSIs: 'localized or systemic condition[s]' resulting from an 'adverse reaction to the presence of an infectious agent(s)' that did not exist at the time of surgery occurring 'within 30 days' of the operative procedure.^{16,17} Patients with post-operative infections were identified from institutional data previously submitted to the National Nosocomial Infections Surveillance database: an ongoing collaborative surveillance system sponsored by the CDC.¹⁸ Using these data, we abstracted microbiology information, including the type of infection (bloodstream infection, gastrointestinal, lower respiratory infection, pneumonia, SSI, skin and soft tissue, and urinary tract infection), species of organism and antibiotic sensitivity.

Because risk factors for post-operative HAIs, in general, differ from those of SSIs specifically, we analysed each outcome separately.¹⁹

Patient demographic information and peri-operative factors known to influence the risk of post-operative infection were also collected. These included: age, race, smoking status, body mass index, malignancy, diabetes, American Society of Anesthesiologists (ASA) physical status, surgical chemoprophylaxis data (type, timing and dose), operative time, blood loss during surgery, an intra-operative red blood cell transfusion and open versus minimally invasive surgery.^{7,20–30}

Statistical analysis

Bivariate analyses of the association between each variable and exposure to pre-operative hospitalization using the Student's t , Pearson χ^2 , and Wilcoxon's rank-sum tests as appropriate were performed. We used univariable logistic regression to calculate unadjusted odds ratios (OR) and 95% confidence intervals (CI) for the association between pre-operative hospitalization and the risk of HAIs and SSIs in particular. Variables with P -values below 0.2 in univariable analyses were included in a final multivariable model to estimate an adjusted OR (aOR) and 95% CI for the association between pre-operative hospitalization and the risk of post-operative infection. For the subgroup of patients with infections, rates of infection with resistant organisms were compared between those with and without a pre-operative hospitalization using the Pearson χ^2 and Fisher's exact tests. We also assessed collinearity using variance inflation factors, evaluated all potential interactions and used the Hosmer–Lemeshow test to assess goodness of fit for the final multivariable models. All analyses were conducted in Stata 13 (StataCorp, College Station, TX, USA). P -values < 0.05 were considered statistically significant.

Results

Patient demographics and characteristics

We identified 1521 adult patients who underwent HPB surgery during the period of study. We excluded patients who had more than one surgery ($n = 90$), patients without HAIs who died before post-operative day 30 ($n = 4$) and those missing variables of interest ($n = 13$). Of the 90 patients excluded for having multiple surgeries, five patients experienced an infection after the second surgery, which was within several months after the first surgery in each case. Our final analysis included 1384 patients meeting both inclusion and exclusion criteria. Of this cohort, 298 (21.5%) had at least one pre-operative hospitalization. Compared with patients who were not hospitalized pre-operatively, these patients were more often diabetic, had a worse ASA status, longer operative times, increased operative blood loss, a greater likelihood of intra-operative blood transfusions, a different surgical chemoprophylaxis profile and less frequent intra-operative re-dosing of surgical chemoprophylaxis in cases where this was indicated (Table 1).

Table 1 Baseline patient characteristics, by history of pre-operative hospitalization

Characteristics	All patients (N = 1384)	Pre-operative hospitalization (N = 298)	No pre-operative hospitalization (N = 1086)	P*
Age, years, median (IQR)	60 (50–70)	61 (51–71)	60 (49–69)	0.182
Male gender, n (%)	678 (49)	154 (52)	524 (48)	0.294
Race, n (%)				
White	1270 (92)	271 (91)	999 (92)	0.295
African-American	67 (5)	19 (6)	48 (4)	
Other	47 (3)	8 (3)	39 (4)	
Body mass index, kg/m ² , median (IQR)	27.2 (24–31)	26.9 (24–32)	27.3 (24–31)	0.969
Operative time, hours, median (IQR)	3.4 (2–5)	4.0 (2–6)	3.3 (2–5)	0.005
Operative blood loss, ml, median (IQR)	150 (40–400)	200 (50–500)	150 (30–400)	0.004
Operative blood transfusion, n (%)	51 (4)	17 (6)	34 (3)	0.037
Malignancy, n (%)	816 (59)	184 (62)	632 (58)	0.270
Diabetes, n (%)	313 (23)	82 (28)	231 (22)	0.020
Open surgery, n (%)	742 (54)	173 (58)	569 (52)	0.083
ASA physical status, n (%)				
1	29 (2)	7 (2)	22 (2)	0.019
2	356 (26)	57 (19)	299 (28)	
3	914 (66)	210 (71)	704 (65)	
4	85 (6)	24 (8)	61 (6)	
Smoking status, n (%)				
Never	641 (46)	125 (42)	516 (48)	0.191
Current	224 (16)	52 (18)	172 (16)	
Former	361 (26)	90 (30)	271 (25)	
Unknown	158 (11)	31 (10)	127 (12)	
Surgical chemoprophylaxis, n (%)				
Ampicillin/sulbactam	869 (63)	165 (55)	704 (65)	0.007
Cefazolin	98 (7)	19 (6)	79 (7)	
Cefoxitin	76 (5)	23 (8)	53 (5)	
Ciprofloxacin	129 (9)	28 (9)	101 (9)	
Piperacillin/tazobactam	78 (6)	25 (8)	53 (5)	
Other	134 (10)	38 (13)	96 (9)	
Re-dosing non-compliance	485 (35)	126 (42)	359 (33)	0.003
Post-operative infections, n (%)	127 (9)	43 (14)	84 (8)	<0.001
Surgical site infections, n (%)	76 (6)	28 (9)	48 (4)	0.001

IQR, interquartile range; SD, standard deviation; ASA, American Society of Anesthesiologists.

*P-values were calculated using Student's T, Wilcoxon rank-sum, and Pearson χ^2 .

Risk of overall infection

Post-operative infection occurred in 127 patients (9.2%); of these, 43 occurred in patients who were hospitalized pre-operatively (14.4%) and 84 occurred in patients who were not hospitalized in the year before surgery (7.7%, $P < 0.001$) (Table 1). Patients who experienced a post-operative infection were more likely to be older, male patients undergoing open surgery for cancer, to experience longer operative times and increased operative blood loss, to have a different

surgical antibiotic prophylaxis profile and less frequent intra-operative re-dosing of surgical chemoprophylaxis in cases where this was indicated. Pre-operative hospitalization was associated with a significantly increased risk of post-operative infection (unadjusted OR 2.01, 95% CI: 1.36–2.98) (Table 2). After adjusting for other covariates, pre-operative hospitalization was significantly associated with an increased risk of post-operative infection (aOR 1.61, 95% CI: 1.06–2.46) (Table 3).

Table 2 Unadjusted risk of post-operative infection, by type of infection

	Any post-operative infection		Surgical site infection	
	OR (95% CI)	P*	OR (95% CI)	P*
Age, years	1.02 (1.01–1.03)	0.002	1.01 (1.00–1.03)	0.162
Male gender	1.68 (1.16–2.44)	0.006	1.96 (1.21–3.17)	0.006
Race		0.403		0.864
White (Reference)	1.00	–	1.00	–
Black	0.45 (0.14–1.45)	0.181	0.79 (0.24–2.58)	0.698
Other	0.89 (0.31–2.53)	0.829	0.75 (0.18–3.16)	0.695
Body mass index, kg/m ²	1.01 (0.98–1.03)	0.718	1.00 (0.97–1.04)	0.809
Operative time, hours	1.35 (1.26–1.44)	<0.001	1.31 (1.22–1.42)	<0.001
Operative blood loss, per 100 ml	1.05 (1.03–1.06)	<0.001	1.04 (1.02–1.06)	<0.001
Operative blood transfusion	1.08 (0.42–2.77)	0.874	–	–
Open surgery	3.22 (2.09–4.94)	<0.001	2.73 (1.61–4.64)	<0.001
Malignancy	3.27 (2.07–5.18)	<0.001	2.74 (1.56–4.80)	<0.001
Diabetes	0.87 (0.55–1.37)	0.549	0.91 (0.52–1.60)	0.738
ASA physical status		0.003		0.065
Physical status 1 (Reference)	1.00	–	1.00	–
Physical status 2	0.64 (0.14–2.91)	0.559	0.47 (0.10–2.21)	0.340
Physical status 3	1.58 (0.37–6.77)	0.534	0.83 (0.19–3.59)	0.804
Physical status 4	2.44 (0.52–11.5)	0.261	1.60 (0.32–7.87)	0.564
Smoking status		0.281		0.096
Never smoker (Reference)	1.00	–	1.00	–
Current smoker	1.39 (0.83–2.31)	0.208	1.87 (1.00–3.50)	0.051
Former smoker	1.36 (0.88–2.12)	0.171	1.62 (0.92–2.85)	0.095
Unknown	1.12 (0.61–2.09)	0.710	1.21 (0.54–2.72)	0.640
Surgical chemoprophylaxis		<0.001		0.005
Cefazolin (Reference)	1.00	–	1.00	–
Ampicillin/sulbactam	1.18 (0.50–2.80)	0.711	1.10 (0.39–3.16)	0.853
Cefoxitin	4.42 (1.65–11.85)	0.003	2.76 (0.80–9.55)	0.108
Ciprofloxacin	0.88 (0.29–2.71)	0.823	0.56 (0.12–2.56)	0.454
Piperacillin/tazobactam	3.07 (1.12–8.50)	0.031	2.69 (0.78–9.28)	0.118
Other	3.01 (1.17–7.74)	0.022	2.48 (0.87–8.60)	0.084
Re-dosing non-compliance	3.45 (2.36–5.03)	<0.001	3.42 (2.11–5.52)	<0.001
Pre-operative hospitalization	2.01 (1.36–2.98)	<0.001	2.24 (1.38–3.64)	0.001

ASA, American Society of Anesthesiologists; CI, confidence interval; OR, odds ratio.

*P-values were calculated using univariable logistic regression.

Risk of surgical site infection

The majority of post-operative infections involved surgical sites (59.8%, $n = 76$). Those experiencing a SSI were more likely to be patients with cancer undergoing open surgery, who experienced longer operative times, increased operative blood loss and less frequent intra-operative re-dosing of surgical chemoprophylaxis in cases where this was indicated. Patients who smoked had a marginally increased risk of SSI. Pre-operative hospitalization was associated with a higher risk of SSI (unadjusted OR 2.24, 95% CI: 1.38–3.64) (Table 2). After adjusting

for other covariates, pre-operative hospitalization was still associated with a significantly increased risk of SSI (aOR 1.79, 95% CI: 1.07–2.97 (Table 3).

Pre-operative hospitalization and antibiotic resistance

Of the patients with post-operative infections, culture sensitivity data were available for 74.8% ($n = 95$). Of the 32 patients with pre-operative hospitalization, 23 had resistant infections. Meanwhile, 31 of the 63 patients who were not hospitalized in the year before surgery developed resistant infections.

Table 3 Adjusted risk of post-operative infection, by type of infection

	Any post-operative infection		Surgical site infection	
	OR (95% CI)	P*	OR (95% CI)	P*
Age, years	1.01 (0.99–1.03)	0.260	1.00 (0.98–1.02)	0.750
Male gender	1.23 (0.82–1.85)	0.321	1.45 (0.87–2.43)	0.157
Operative time, hours	1.17 (1.07–1.29)	0.001	1.15 (1.03–1.29)	0.014
Operative blood loss (per 100 ml)	1.01 (0.99–1.03)	0.425	1.01 (0.98–1.03)	0.577
Malignancy	1.67 (0.99–2.83)	0.054	1.57 (0.82–3.01)	0.175
ASA physical status		0.299		0.334
Physical status 1 (Reference)	1.00	–	1.00	–
Physical status 2	0.36 (0.07–1.91)	0.231	0.26 (0.05–1.45)	0.126
Physical status 3	0.58 (0.11–2.99)	0.511	0.29 (0.05–1.61)	0.158
Physical status 4	0.70 (0.12–4.20)	0.700	0.44 (0.07–2.88)	0.393
Smoking status		0.955		0.454
Never smoker (Reference)	1.00	–	1.00	–
Current smoker	1.13 (0.65–1.98)	0.659	1.66 (0.85–3.25)	0.140
Former smoker	1.07 (0.66–1.74)	0.777	1.37 (0.75–2.52)	0.305
Unknown	0.95 (0.49–1.83)	0.868	1.04 (0.45–2.44)	0.921
Surgical chemoprophylaxis		0.003		0.044
Cefazolin (Reference)	1.00	–	1.00	–
Cefoxitin	1.43 (0.48–4.22)	0.520	0.83 (0.22–3.18)	0.788
Ampicillin/sulbactam	0.67 (0.26–1.72)	0.411	0.64 (0.21–1.98)	0.439
Ciprofloxacin	0.97 (0.29–3.23)	0.965	0.69 (0.14–3.43)	0.650
Piperacillin/tazobactam	1.56 (1.30–5.13)	0.431	1.32 (0.34–5.03)	0.687
Other	2.38 (0.82–6.87)	0.109	2.46 (0.68–8.90)	0.169
Re-dosing noncompliance	2.15 (1.12–4.13)	0.021	2.47 (1.09–5.58)	0.030
Pre-operative hospitalization	1.61 (1.06–2.46)	0.026	1.79 (1.07–2.97)	0.026

CI, confidence interval; OR, adjusted odds ratio; ASA, American Society of Anesthesiologists.

*P-values were calculated using multivariable logistic regression analyses. Open surgery was not included as a result of collinearity.

Pre-operative hospitalization was associated with a significantly higher risk of antibiotic-resistant post-operative infection ($P = 0.035$).

Culture sensitivity data were available for 65 patients with SSIs. Of the 24 patients with SSIs who were hospitalized in the year before surgery, 19 of these had resistant infections. In contrast, 20 of the 41 patients with SSIs who were not hospitalized in the year before surgery had resistant SSIs. Pre-operative hospitalization was also significantly associated with an increased risk of SSIs as a result of microorganisms resistant to prophylactic antibiotics ($P = 0.016$).

Finally, for each type of organism cultured from these infections, we determined whether preoperative hospitalization was associated with higher rates of antibiotic-resistance (vs. sensitivity). Patients with a pre-operative hospitalization were more likely to develop an antibiotic-resistant (versus sensitive) infection with enterococcus ($P = 0.001$) or lactose-fermenting bacteria ($P = 0.048$) than patients without a pre-operative hospitalization (Table 4). However, among those with a

staphylococcal infection or infection with gram-negative rods, pre-operative hospitalization was not associated with a higher rate of antibiotic-resistant infections (Table 4).

Among patients who developed SSIs, patients with a pre-operative hospitalization were more likely than those without a pre-operative hospitalization to develop antibiotic-resistant infections with enterococcal species ($P < 0.001$), gram-negative rods ($P < 0.001$), or lactose-fermenting bacteria ($P = 0.001$, Table 4). There were no significant differences observed in rates of antibiotic-resistant infections with anaerobic and non-lactose fermenting gram-negative organisms in those with pre-operative hospitalization when compared with those without pre-operative hospitalization (Table 4).

Discussion

In this study, pre-operative hospitalization was associated with a significantly higher risk of developing a post-operative resistant HAI, including resistant SSIs. These findings contribute to

Table 4 Organisms resistant to pre-operative antibiotic prophylaxis

	Overall resistant, n (%)			Resistant SSI, n (%)		
	Pre-operative Hospitalization	No Pre-operative Hospitalization	P*	Pre-operative Hospitalization	No Pre-operative Hospitalization	P*
Gram-positive cocci	15 (52)	22 (47)	0.488	13 (62)	15 (43)	0.195
Genus <i>Staphylococcus</i>	5 (42)	20 (63)	0.076	4 (40)	14 (58)	0.299
Genus <i>Enterococcus</i>	10 (67)	2 (15)	0.001	9 (75)	1 (11)	<0.001
Gram-negative rods	19 (63)	20 (34)	0.053	15 (75)	6 (20)	<0.001
Lactose-fermenting	15 (68)	14 (31)	0.048	13 (81)	5 (22)	0.001
Non-lactose-fermenting	4 (57)	6 (38)	0.746	2 (50)	1 (20)	0.290
Anaerobes	1 (25)	0 (0)	1.000	1 (25)	0 (0)	1.000

SSI, surgical-site infection.

*P-values were calculated using Pearson χ^2 and Fisher's exact test.

a growing body of literature suggesting that resistant organisms colonize patients during prior hospitalization.^{13,14,31,32} MRSA nasal carriage, for example, is a risk factor for MRSA SSI whereas testing positive for VRE increases the risk of VRE infection.^{33–37} Several previous studies found that patients admitted from the community with resistant infections were more likely to have a history of hospitalization, but did not focus on surgical patients or post-operative infections.^{8,15,38} Mahajan *et al.* incidentally found an association between SSI and patients with cancer hospitalized up to 1 year before gastrointestinal surgery, but this association was not examined in detail and has not previously been demonstrated in patients undergoing HPB surgery.³⁹

The majority of infections among patients with pre-operative hospitalization involved microorganisms that were resistant to surgical chemoprophylaxis, suggesting these patients represent a high-risk population. Multiple studies agree that patients with known colonization with resistant organisms or those at a high risk of post-operative infection should receive broader prophylactic antibiotic coverage, yet these studies do not support a specific antibiotic prophylaxis strategy.^{40,41} For patients undergoing HPB surgery, adequate prophylactic coverage of MRSA reduces the incidence MRSA infection, yet vancomycin, for example, increases the risk of SSI for those not colonized.^{7,42} Concerning a strategy that expands chemoprophylaxis post-operatively, Ren *et al.*⁴³ demonstrated no difference in SSI rates within a 30-day post-operative period after HPB surgery.

In addition to pre-operative hospitalization, our findings add to the existing body of literature showing that failure to re-dose surgical chemoprophylaxis intra-operatively (re-dosing non-compliance) increases the risk for post-operative infection and SSI.^{26–29} Current recommendations include instructions to re-dose prophylactic antibiotics intra-operatively if the duration of the operation exceeds two half-lives of the antibiotic. For example, the half-lives of cefoxitin and piperacillin–tazobactam are 0.7–1.1 and 0.7–1.2 h, which translate into re-dosing intervals of 2–3 h after the initial dose.^{21,26,40,44–47}

However, despite evidence to support the appropriateness of current surgical chemoprophylaxis guidelines, there is a substantial gap between these guidelines and their implementation in daily practice.^{48–50} Studies show that antibiotic re-dosing was found to have the greatest overall non-compliance in SSI prophylaxis and could reflect a lack of understanding of dosing practices.^{26,50} Although our local institutional guidelines reflect current guidelines, we found that re-dosing non-compliance remains prevalent in our institution's chemoprophylaxis practices; and it is likely that we are not maintaining adequate antibiotic levels in the circulation of patients who undergo lengthy surgeries. Re-dosing recommendations may impose an added task burden in the operating room during busy surgeries, especially for antibiotics with relatively short half-lives. Measures such as improving awareness of current re-dosing guidelines or procedure-driven prompts for antibiotic selection in documentation software that include reminders in the operating room to re-dose antibiotics at specific times may be helpful.

We acknowledge several limitations to the present study. Data contained in some inpatient electronic medical records are not comprehensive; however, we cross-referenced these records with scanned paper documents when available to maximize accuracy. Some patients who had post-operative infections may not have sought medical attention or could have been evaluated outside of our institution. Additionally, we may not have captured some pre-operative hospitalizations at outside hospitals if these were not clearly documented in the clinical notes within our electronic medical record system. There could also have been some selection bias; pre-operative hospitalization is likely a surrogate for severity of illness and comorbid conditions, which require therapy and/or inpatient workup. However, we adjusted for all known covariates that may account for these differences in illness.

In summary, our results show that pre-operative hospitalization is associated with an increased incidence of post-operative infections with hospital-acquired organisms that are resistant to standard surgical chemoprophylaxis. In many instances,

pre-operative hospitalization cannot be avoided or has occurred before surgery becomes necessary. In these cases, it is important to focus on other modifiable risk factors to reduce the risk of post-operative infection, such as timely re-dosing of intra-operative antibiotics and broader prophylactic coverage. For HPB diseases, in particular, many patients require extensive diagnostic or therapeutic procedures prior to surgery. While inpatient evaluation may improve the efficiency of a pre-operative workup, this needs to be balanced with the potentially increased risk of infection. To build on these results, we plan to conduct cost analyses, analyse a larger series of patients and focus on identifying high-risk populations that may benefit from broad-spectrum antibiotic prophylaxis. We also plan to identify patients who underwent diagnostic and therapeutic procedures during pre-operative hospitalizations related to their primary HPB disease and to examine whether these patients represent a higher risk population when compared with those hospitalized for other reasons. Ultimately, our results suggest that patients with a history of hospitalization may represent a high-risk group in which current infection control measures are not sufficient to prevent post-operative HAIs.

Funding sources

None.

References

- Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. (1999) The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 20:725–730.
- Correa-Gallego C, Gonen M, Fischer M, Grant F, Kemeny NE, Arslan-Carlson V *et al.* (2013) Perioperative complications influence recurrence and survival after resection of hepatic colorectal metastases. *Ann Surg Oncol* 20:2477–2484.
- Haruki K, Shiba H, Fujiwara Y, Furukawa K, Wakiyama S, Ogawa M *et al.* (2013) Negative impact of surgical site infection on long-term outcomes after hepatic resection for colorectal liver metastases. *Anticancer Res* 33:1697–1703.
- Urban JA. (2006) Cost analysis of surgical site infections. *Surg Infect (Larchmt)* 7(Suppl 1):S19–S22.
- de Lissoyoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. (2009) Surgical site infection: incidence and impact on hospital utilization and treatment costs. *Am J Infect Control* 37:387–397.
- Sparling KW, Ryckman FC, Schoettker PJ, Byczkowski TL, Helpling A, Mandel K *et al.* (2007) Financial impact of failing to prevent surgical site infections. *Qual Manag Health Care* 16:219–225.
- Al-Mukhtar A, Wong VK, Malik HZ, Abu-Hilal M, Denton M, Wilcox M *et al.* (2009) A simple prophylaxis regimen for MRSA: its impact on the incidence of infection in patients undergoing liver resection. *Ann R Coll Surg Engl* 91:35–38.
- Cardoso T, Ribeiro O, Aragao IC, Costa-Pereira A, Sarmiento AE. (2012) Additional risk factors for infection by multidrug-resistant pathogens in healthcare-associated infection: a large cohort study. *BMC Infect Dis* 12:375.
- Rezende NA, Blumberg HM, Metzger BS, Larsen NM, Ray SM, McGowan JE Jr. (2002) Risk factors for methicillin-resistance among patients with *Staphylococcus aureus* bacteremia at the time of hospital admission. *Am J Med Sci* 323:117–123.
- Furuno JP, Perencevich EN, Johnson JA, Wright MO, McGregor JC, Morris JG Jr *et al.* (2005) Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococci* co-colonization. *Emerg Infect Dis* 11:1539–1544.
- Han SH, Chin BS, Lee HS, Jeong SJ, Choi HK, Kim CK *et al.* (2009) Recovery of both vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus* from culture of a single clinical specimen from colonized or infected patients. *Infect Control Hosp Epidemiol* 30:130–138.
- Siegel JD, Rhinehart E, Jackson M, Chiarello L, Healthcare Infection Control Practices Advisory Committee. (2007) Management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control* 35:S165–S193.
- Hidron AI, Kourbatova EV, Halvosa JS, Terrell BJ, McDougal LK, Tenover FC *et al.* (2005) Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients admitted to an urban hospital: emergence of community-associated MRSA nasal carriage. *Clin Infect Dis* 41:159–166.
- Zacharioudakis IM, Zervou FN, Ziakas PD, Rice LB, Mylonakis E. (2015) Vancomycin-resistant enterococci colonization among dialysis patients: a meta-analysis of prevalence, risk factors, and significance. *Am J Kidney Dis* 65:88–97.
- Chen SY, Wu GH, Chang SC, Hsueh PR, Chiang WC, Lee CC *et al.* (2008) Bacteremia in previously hospitalized patients: prolonged effect from previous hospitalization and risk factors for antimicrobial-resistant bacterial infections. *Ann Emerg Med* 51:639–646.
- Horan TC, Andrus M, Dudeck MA. (2008) CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 36:309–332.
- Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. (1992) CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 13:606–608.
- Emori TG, Culver DH, Horan TC, Jarvis WR, White JW, Olson DR *et al.* (1991) National nosocomial infections surveillance system (NNIS): description of surveillance methods. *Am J Infect Control* 19:19–35.
- Pessaux P, Msika S, Atalla D, Hay JM, Flamant Y, French Association for Surgical Research. (2003) Risk factors for postoperative infectious complications in noncolorectal abdominal surgery: a multivariate analysis based on a prospective multicenter study of 4718 patients. *Arch Surg* 138:314–324.
- Haley RW, Hooton TM, Culver DH, Stanley RC, Emori TG, Hardison CD *et al.* (1981) Nosocomial infections in U.S. hospitals, 1975–1976: estimated frequency by selected characteristics of patients. *Am J Med* 70:947–959.
- Page CP, Bohnen JM, Fletcher JR, McManus AT, Solomkin JS, Wittmann DH. (1993) Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. *Arch Surg* 128:79–88.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. (1999) Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 20:250–278.

23. Yang T, Tu PA, Zhang H, Lu JH, Shen YN, Yuan SX *et al.* (2014) Risk factors of surgical site infection after hepatic resection. *Infect Control Hosp Epidemiol* 35:317–320.
24. Ceppa EP, Pitt HA, House MG, Kilbane EM, Nakeeb A, Schmidt CM *et al.* (2013) Reducing surgical site infections in hepatopancreatobiliary surgery. *HPB (Oxford)* 15:384–391.
25. Nanashima A, Arai J, Oyama S, Ishii M, Abo T, Wada H *et al.* (2014) Associated factors with surgical site infections after hepatectomy: predictions and countermeasures by a retrospective cohort study. *Int J Surg* 12:310–314.
26. Miliani K, L'Heriteau F, Astagneau P, Group INS. (2009) Non-compliance with recommendations for the practice of antibiotic prophylaxis and risk of surgical site infection: results of a multilevel analysis from the INCISO Surveillance Network. *J Antimicrob Chemother* 64:1307–1315.
27. Zanetti G, Giardina R, Platt R. (2001) Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. *Emerg Infect Dis* 7:828–831.
28. Scher KS. (1997) Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg* 63:59–62.
29. DiPiro JT, Vallner JJ, Bowden TA Jr, Clark BA, Sisley JF. (1985) Intraoperative serum and tissue activity of cefazolin and cefoxitin. *Arch Surg* 120:829–832.
30. Lopez-Ben S, Palacios O, Codina-Barreras A, Albiol MT, Falgueras L, Castro E *et al.* (2014) Pure laparoscopic liver resection reduces surgical site infections and hospital stay. Results of a case-matched control study in 50 patients. *Langenbecks Arch Surg* 399:307–314.
31. Loo VG, Bourgault AM, Poirier L, Lamothe F, Michaud S, Turgeon N *et al.* (2011) Host and pathogen factors for *Clostridium difficile* infection and colonization. *N Engl J Med* 365:1693–1703.
32. Beezhold DW, Slaughter S, Hayden MK, Matushek M, Nathan C, Trenholme GM *et al.* (1997) Skin colonization with vancomycin-resistant enterococci among hospitalized patients with bacteremia. *Clin Infect Dis* 24:704–706.
33. Kluytmans JA, Mouton JW, Ijzerman EP, Vandenbroucke-Grauls CM, Maat AW, Wagenvoort JH *et al.* (1995) Nasal carriage of *Staphylococcus aureus* as a major risk factor for wound infections after cardiac surgery. *J Infect Dis* 171:216–219.
34. Goyal N, Miller A, Tripathi M, Parvizi J. (2013) Methicillin-resistant *Staphylococcus aureus* (MRSA): colonisation and pre-operative screening. *Bone Joint J* 95B:4–9.
35. Perl TM, Golub JE. (1998) New approaches to reduce *Staphylococcus aureus* nosocomial infection rates: treating *S. aureus* nasal carriage. *Ann Pharmacother* 32:S7–S16.
36. Reichman DE, Greenberg JA. (2009) Reducing surgical site infections: a review. *Rev Obstet Gynecol* 2:212–221.
37. Liou DZ, Barmparas G, Ley EJ, Salim A, Tareen A, Casas T *et al.* (2014) To swab or not to swab? A prospective analysis of 341 SICU VRE screens. *J Trauma Acute Care Surg* 76:1192–1200.
38. Micek ST, Kollef KE, Reichley RM, Roubinian N, Kollef MH. (2007) Health care-associated pneumonia and community-acquired pneumonia: a single-center experience. *Antimicrob Agents Chemother* 51:3568–3573.
39. Mahajan SN, Ariza-Heredia EJ, Rolston KV, Graviss LS, Feig BW, Aloia TA *et al.* (2014) Perioperative antimicrobial prophylaxis for intra-abdominal surgery in patients with cancer: a retrospective study comparing ertapenem and nonertapenem antibiotics. *Ann Surg Oncol* 21:513–519.
40. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK *et al.* (2013) Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt)* 14:73–156.
41. Yanni F, Mekhail P, Morris-Stiff G. (2013) A selective antibiotic prophylaxis policy for laparoscopic cholecystectomy is effective in minimising infective complications. *Ann R Coll Surg Engl* 95:345–348.
42. Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KM. (2011) Preoperative nasal methicillin-resistant *Staphylococcus aureus* status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. *Infect Control Hosp Epidemiol* 32:791–796.
43. Ren J, Bao L, Niu J, Wang Y, Ren X. (2013) Prophylactic antibiotics used in patients of hepatobiliary surgery. *Pak J Med Sci* 29:1199–1202.
44. Bratzler DW, Houck PM, Surgical Infection Prevention Guideline Writers Workgroup. (2005) Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Am J Surg* 189:395–404.
45. File TM Jr. (2013) New guidelines for antimicrobial prophylaxis in surgery. *Infect Dis Clin Pract (Baltim Md)* 21:185–186.
46. Alexander JW, Solomkin JS, Edwards MJ. (2011) Updated recommendations for control of surgical site infections. *Ann Surg* 253:1082–1093.
47. Stratchounski LS, Taylor EW, Dellinger EP, Pechere JC. (2005) Antibiotic policies in surgery: a consensus paper. *Int J Antimicrob Agents* 26:312–322.
48. Lallemand S, Thouverez M, Bailly P, Bertrand X, Talon D. (2002) Non-observance of guidelines for surgical antimicrobial prophylaxis and surgical-site infections. *Pharm World Sci* 24:95–99.
49. Tourmousoglou CE, Yiannakopoulou E, Kalapothaki V, Bramis J, St Papadopoulos J. (2008) Adherence to guidelines for antibiotic prophylaxis in general surgery: a critical appraisal. *J Antimicrob Chemother* 61:214–218.
50. Goede WJ, Lovely JK, Thompson RL, Cima RR. (2013) Assessment of prophylactic antibiotic use in patients with surgical site infections. *Hosp Pharm* 48:560–567.